

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
14 October 2004 (14.10.2004)

PCT

(10) International Publication Number
WO 2004/087935 A3

(51) International Patent Classification⁷: C12P 7/62, 17/06,
C07C 67/00, A61K 31/215 // (C12P 7/62, C12R 1:465)

(21) International Application Number:
PCT/IB2004/001003

(22) International Filing Date: 1 April 2004 (01.04.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
559/DEL/2003 1 April 2003 (01.04.2003) IN

(71) Applicant (for all designated States except US): **RAN-
BAXY LABORATORIES LIMITED** [IN/IN]; 19, Nehru
Place, New Delhi 110 019, Delhi (IN).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **KUMAR, Parveen**
[IN/IN]; 95, Sector 11, Panchkula, Haryana 134112 (IN).
KATIAL, Vikas [IN/IN]; #1381, Sector - 29, Noida,
Uttar Pradesh 201303 (IN). **GIGRAS, Paresh** [IN/IN];
c/o Shri Jagdish Chander Jitender Kumar, Chauraha
Gali, Muradabad, Uttar Pradesh 244001 (IN). **KUMAR,
Sudeep** [IN/IN]; B-107 Alaknanda Apt., Rampuri, Surya
Nagar, Ghaziabad, Uttar Pradesh 201011 (IN). **SHUKLA,
Aniruddha** [IN/IN]; #6148/5, Sector - D, Pocket - 6,
Vasant Kunj, New Delhi 110070 (IN).

(74) Common Representative: **RANBAXY LABORATO-
RIES LIMITED**; c/o DESHMUKH, Jay, R., 600 College
Road East, Suite 2100, Princeton, NJ 08540 (US).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
ZW.

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), Euro-
pean (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR,
GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK,
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments

(88) Date of publication of the international search report:
13 January 2005

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: FERMENTATION PROCESS FOR THE PREPARATION OF PRAVASTATIN

(57) Abstract: The invention relates to a fermentation process for the preparation of substantially pure pravastatin. The process provides a method of producing pravastatin by microbial hydroxylation of compactin (ML-236B) by maintaining a concentration of compactin at not less than 300 µg /ml during the process. The process produces substantially pure pravastatin with reduced related impurities. The invention also relates to pharmaceutical compositions that include the substantially pure pravastatin.

WO 2004/087935 A3

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12P7/62 C12P17/06 C07C67/00 A61K31/215
//(C12P7/62,C12R1:465)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12P C07C A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, BIOSIS, WPI Data, PAJ, FSTA

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98/45410 A (YUNGJIN PHARMACEUTICAL IND CO ; KIM JI YOON (KR); LEE JOO KYUNG (KR);) 15 October 1998 (1998-10-15) page 9, line 15 - line 27; claims 2,4	1-22
P,X	PARK JOO-WOONG ET AL: "Bioconversion of compactin into pravastatin by Streptomyces sp." BIOTECHNOLOGY LETTERS, vol. 25, no. 21, November 2003 (2003-11), pages 1827-1831, XP008033522 ISSN: 0141-5492 the whole document ----- -/--	1-22

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

18 October 2004

Date of mailing of the international search report

01.11.2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Devijver, K

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	HOSOBUCHI M ET AL: "APPLICATION OF COMPUTER TO MONITORING AND CONTROL OF FERMENTATION PROCESS: MICROBIAL CONVERSION OF ML-236B NA TO PRAVASTATIN" BIOTECHNOLOGY AND BIOENGINEERING, INTERSCIENCE PUBLISHERS, LONDON, GB, vol. 42, no. 7, 1993, pages 815-820, XP002036625 ISSN: 0006-3592 cited in the application the whole document	1-22
A	US 2002/081675 A1 (HORVATH GYULA ET AL) 27 June 2002 (2002-06-27) cited in the application	1-22
X	page 1 - page 2 page 5, paragraph 36 page 6, paragraph 44; example 2	23-25
A	US 2001/026934 A1 (YASHPHE JACOB ET AL) 4 October 2001 (2001-10-04) cited in the application the whole document	1-22
A	WO 00/17182 A (LEK TOVARNA FARMACEVTSKIH ; MILIVOJEVIC DUSAN (SI); BASTARDA ANDREJ (S) 30 March 2000 (2000-03-30) abstract; claims 26-29; examples 1-5	1-22
X	GRAHEK R ET AL: "Chromatographic purification of some 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors" JOURNAL OF CHROMATOGRAPHY, ELSEVIER SCIENCE PUBLISHERS B.V. AMSTERDAM, NL, vol. 918, no. 2, 25 May 2001 (2001-05-25), pages 319-324, XP004239132 ISSN: 0021-9673 the whole document	23-25
X	DATABASE WPI Section Ch, Week 200250 Derwent Publications Ltd., London, GB; Class B05, AN 2002-471387 XP002301127 -& JP 2002 128739 A (SANKYO CO LTD) 9 May 2002 (2002-05-09) abstract	23-25

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9845410	A	15-10-1998	KR 210482 B1 CN 1254373 A , B EP 0975738 A1 JP 2001519654 T WO 9845410 A1 US 6306629 B1	15-07-1999 24-05-2000 02-02-2000 23-10-2001 15-10-1998 23-10-2001
US 2002081675	A1	27-06-2002	US 6682913 B1 EP 1279695 A1 US 2003207413 A1 US 2004039225 A1 AU 774438 B2 AU 3356700 A BG 105778 A BR 0009180 A CA 2361701 A1 CN 1347400 T CZ 20012761 A3 EP 1154979 A1 HR 20010577 A1 HU 0200650 A2 JP 2002535977 T NO 20013818 A PL 350317 A1 SK 10932001 A3 TR 200103127 T2 WO 0046175 A1 ZA 200106359 A	27-01-2004 29-01-2003 06-11-2003 26-02-2004 24-06-2004 25-08-2000 31-05-2002 26-03-2002 10-08-2000 01-05-2002 15-05-2002 21-11-2001 31-12-2002 28-08-2002 29-10-2002 03-10-2001 02-12-2002 04-06-2002 22-04-2002 10-08-2000 02-08-2002
US 2001026934	A1	04-10-2001	US 6274360 B1 US 5942423 A US 2003199075 A1 CA 2223122 A1 EP 0836642 A1 JP 11508239 T WO 9640863 A1	14-08-2001 24-08-1999 23-10-2003 19-12-1996 22-04-1998 21-07-1999 19-12-1996
WO 0017182	A	30-03-2000	SI 20072 A AU 766630 B2 AU 5528499 A BG 105348 A CA 2343645 A1 CN 1318063 T EP 1114040 A1 HR 20010045 A1 HU 0102997 A2 WO 0017182 A1 JP 2002526486 T NZ 509582 A PL 345883 A1 SK 20022000 A3 US 2004138294 A1 US 6695969 B1	30-04-2000 23-10-2003 10-04-2000 30-11-2001 30-03-2000 17-10-2001 11-07-2001 31-12-2001 28-12-2001 30-03-2000 20-08-2002 31-10-2003 14-01-2002 06-08-2001 15-07-2004 24-02-2004
JP 2002128739	A	09-05-2002	JP 3463875 B2	05-11-2003